September 15, 2003

Bruce Katje
Regulatory Compliance Manager
ESCO Company Limited Partnership
2340 Roberts Street
P.O. Box 448
Muskegon, MI 49443

Dear Mr. Katje:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for the Color Former Category posted on the ChemRTK HPV Challenge Program Web site on May 15, 2003. I commend ESCO Company Limited Partnership for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that ESCO advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Color Former Category

SUMMARY OF EPA COMMENTS

The sponsors, ESCO Company Limited Partnership, submitted a test plan and robust summaries to EPA for the Color Former category dated May 2, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on May 15, 2003. The category consists of 6'-(diethylamino)-3'-methyl-2'-(2,4-dimethylphenylamino)spiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one (Black XV, CAS # 36431-22-8); 6'-(diethylamino)-3'-methyl-2'-(phenylamino)spiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one (N-102, CAS #29512-49-0); and 6'-(dibutylamino)-3'-methyl-2'-(phenylamino)spiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one (ODB-2, CAS # 89331-94-2).

EPA has reviewed this submission and has reached the following conclusions:

1. Category Justification. The category justification is adequate.

2. Physicochemical Properties. The submitter needs to provide estimated boiling point data for these chemicals.

3. Environmental Fate. The submitter needs to provide measured data for stability in water for Black XV. The submitter also needs to provide input values in the fugacity robust summary.

4. Health Effects. Although data are available for acute and genetic toxicity endpoints on all three compounds and the submitter's plan to use ODB-2 data to address data gaps on the repeated-dose and reproduction toxicity endpoints is acceptable, the adequacy of the ODB-2 data can not be determined until the submitter provides the purity of the tested substances. In addition, the submitter needs to provide a separate robust summary to address the developmental toxicity endpoint and address deficiencies in the robust summaries.

5. Ecological Effects. Adequate data are available for fish, aquatic invertebrates, and algae for the purposes of the HPV Challenge program.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON THE COLOR FORMER CATEGORY CHALLENGE SUBMISSION

Category Definition

The category definition is clear and unambiguous.

Category Justification

The submitter justifies the color former category on the basis of similar chemical structures and comparable physicochemical, environmental fate, and ecological and mammalian toxicological properties for all three compounds. EPA agrees with this justification and with the submitter's plan to use a read-across approach to address data gaps for repeated-dose, reproduction and developmental toxicity endpoints with the submitted ODB-2 data.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient, and water solubility)

The data provided by the submitter for melting point, vapor pressure, octanol/water partition coefficient and water solubility are adequate for the purposes of the HPV Challenge Program.

Boiling point. In the robust summary, the submitter only indicates that these chemicals melt at temperatures above 168 °C, and that no boiling point data have been generated. Although measured boiling point data are needed for these chemicals, their high melting points suggest that these chemicals will boil or decompose at very high temperatures. According to OECD guidelines, if boiling points of chemicals exceed 300 °C, estimated values will be acceptable.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

The data provided by the submitter for photodegradation, biodegradation and fugacity are adequate for the purposes of the HPV Challenge Program.

Stability in water. The submitter obtained the reported half-life values of 150, 150, and 60 days for Black XV, N-102, and ODB-2, respectively, from EPIWIN. EPA notes that these values are derived from the Level III model in EPIWIN from the BIOWIN estimates and are not related to hydrolysis. Although EPA agrees with the submitter that HYDROWIN v1.67 would not estimate a hydrolysis rate constant for this class of compounds, these chemicals contain a cyclic ester group that may be susceptible to hydrolysis. Therefore, the submitter needs to provide measured stability in water data for Black XV following OECD Guideline 111.

Fugacity. The submitter needs to include the input values used in the model in the fugacity robust summary.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Although data are available for acute and genetic toxicity endpoints on all three compounds and the submitter's plan to use ODB-2 data to address data gaps on the repeated-dose, reproduction, and developmental toxicity endpoints is acceptable, the adequacy of these data can not be determined until the submitter provides critical information in robust summaries, specifically the purity of the tested substance. The submitter also needs to address deficiencies in the robust summaries.

Acute Toxicity. The test plan matrix (Table 1) incorrectly indicated that an acute dermal toxicity study was available for N-102. No robust summary was submitted for this compound, as correctly indicated in Toxicological Data Table 5. The submitter needs to address this discrepancy.

Genetic Toxicity. EPA reserves judgement on the adequacy of the data submitted for bacterial mutagenicity and *in vitro* chromosomal aberration pending receipt of amended robust summaries. If this information is not available, additional testing of Black XV or N-102 will be needed.

Developmental Toxicity. The submitter used a one-generation reproduction toxicity study on ODB-2 that includes pertinent developmental toxicity information to address the developmental toxicity data gap. The submitter needs to provide this information in a separate robust summary for this endpoint.

Ecological Effects (fish, invertebrates, and algae)

Adequate data are available for fish, aquatic invertebrates, and algae for the purposes of the HPV Challenge program.

Specific Comments on the Robust Summaries

Generic comment

The submitter needs to consult EPA guidance documents for the preparation of robust summaries (http://www.epa.gov/opptintr/chemrtk/guidocs.htm). Each summary needs to include the purity of the tested substance.

Health Effects

Acute Toxicity. For Black XV robust summaries need to include the results of body weight examination.

Repeated-Dose Toxicity. A summary for the 28-day gavage assay of ODB-2 lacked the magnitude of the reduction in adrenal weights in high-dose females. The latter information is needed to evaluate the identification of 1000 mg/kg/day as a NOAEL.

Genetic Toxicity. Robust summaries for bacterial gene mutation assays need the following missing information: positive control data, the number of replicates and the criteria for judging the results.

The summaries for *in vitro* chromosomal aberration assays for all three compounds lack the following information: culture harvest time, number of metaphases examined per concentration, cytotoxic concentration (the summary mistakenly put genotoxicity results in that field), positive controls, and criteria for determining positive results (OECD guidance indicates that statistical criteria alone are not sufficient).

Reproductive Toxicity. All results of this study are provided as qualitative statements such as “similar to those of control animals.” The submitter needs to provide quantitative data in a tabular form in order for EPA to assess the adequacy of these data. Also, if available, the submitter needs to provide the number of corpora lutea, whether or not histopathological evaluation of reproductive organs was conducted and the specific results of this evaluation.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.